

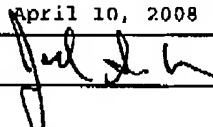

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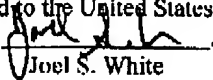
<b>PRE-APPEAL BRIEF REQUEST FOR REVIEW</b>		Docket Number (Optional) <b>CL1496ORD</b>	<b>APR 10 2008</b>
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		First Named Inventor <b>Michele CARGILL</b>	
		Art Unit <b>1634</b>	Examiner <b>Juliet C. SWITZER</b>
Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.			
This request is being filed with a notice of appeal.			
The review is requested for the reason(s) stated on the attached sheet(s). Note: No more than five (5) pages may be provided.			
I am the <input type="checkbox"/> applicant/inventor. <input type="checkbox"/> assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/98) <input checked="" type="checkbox"/> attorney or agent of record. Registration number <u>41,420</u>		<u></u> Signature <b>Ben Wang</b> Typed or printed name <u>510.749.4378</u> Telephone number <u>April 10, 2008</u> Date	
<input type="checkbox"/> attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____			
NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below.			
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This collection of information is required by 35 U.S.C. 132. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11, 1.14 and 41.6. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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Atty. Docket: CL1496ORD

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**APR 10 2008**

In re Application of: Cargill, et al.

Art Unit: 1634

Serial No.: 10/719,993

Examiner: SWITZER, Juliet Caroline

Filed: November 24, 2003

Atty. Docket No.: CL1496ORD

For: GENETIC POLYMORPHISMS  
ASSOCIATED WITH ALZHEIMER'S  
DISEASES, METHODS OF DETECTION  
AND USES THEREOF

Submission Accompanying Pre-Appeal Brief Request

Submission Accompanying Pre-Appeal Brief Request

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Sir:

This response contains remarks accompanying the Pre-Appeal Brief Request, which is filed concurrently with the Notice of Appeal for the above-identified application. The Notice of Appeal is filed in response to the Final Office Action mailed December 10, 2007, setting a three month period for response. This Final Office Action was supposed to have been mailed August 13, 2007, but did not reach Applicants due to an incorrect address. Applicants hereby submit a Petition for an Extension of Time of one month in which to respond to the Final Office Action, thus making this response timely.

REMARKS

Status of the Claims

Claims 1 and 36-70 are currently pending, as presented in the Supplemental Amendment filed May 25, 2007. Reference is also made to the Amendment and Remarks filed April 6, 2007.

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**The Sole Remaining Rejection is Clearly Erroneous**

The only rejection in the Final Office Action (hereinafter "FOA") relates to 35 USC §112, first paragraph, for allegedly lacking of enablement.

Applicants respectfully believe that the rejection is clearly not proper and are without basis for the following reasons:

**Individual vs. human**

The Examiner states that the "specification and the art do not provide any guidance that the polymorphic SNP is present in other animals or individuals" other than humans. See FOA, at page 5.

This argument is moot because the pending claims are directed towards humans.

**One SNP vs. other SNPs**

The Examiner also states that it "is unpredictable that there are any other SNPs in SEQ ID NO: 7368 and the location of the SNPs if there are SNPs". See FOA, at page 5.

This argument is irrelevant because the pending claims are directed towards only one SNP at the present time.

**Increased Risk vs. Decreased Risk**

The Examiner alleges that the specification does "not provide what the increase or decrease is in relation to." See FOA, at page 6.

The studies in the present invention use Odds Ratio (OR) in determining whether one of the two alleles being tested is a risk allele. Namely, if the OR is larger than 1, the reported allele associated with that OR is considered a risk allele relative to the other allele. Conversely, the other allele would be the non-risk allele relative to the risk allele. Applicants teach as such in the Example section of the specification, at page 118-120, and in Table 6. This concept is also well known in the art and used commonly in studies with case-control samples.

**The Hirschhorn reference**

The Examiner cites *Hirschhorn* in supporting the lack of enablement rejection, stating that Hirschhorn "teaches that most reported associations are not robust." See FOA, page 3.

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However, this argument does NOT logically support the allegation that the instant invention is not reliable. The mere fact that OTHER association studies were not easily reproduced does NOT cast doubt on the reliability of the instantly claimed invention. As taught in *Hirschhorn*, many factors could cause the other studies to fail, factors that are not present in the instant invention.

In fact, the same statement quoted by the Examiner that "*Hirschhorn* cautions in drawing conclusions from a single report of an association between a genetic variant and disease susceptibility" tends to bolster the reliability of the instant invention. FOA, page 4 (emphasis added). That is because the current claimed SNP has been replicated in four large, well-characterized case-control samples. See Grupe et al, *The American Journal of Human Genetics*, Vol. 79, at page 183.

The Ioannidis reference

To support her lack of enablement rejection, the Examiner cites *Ioannidis* stating that "the results of the first study correlate only modestly with subsequent research on the same association". See FOA, page 4.

On the contrary, this argument actually strengthens the reliability of Applicants' invention because the instantly claimed SNP has been replicated in more than "one" sample, four to be exact. See Grupe, at page 183.

The Bertram reference

The Examiner doubts the reliability of the instant invention by citing Bertram et al because Bertram failed to replicate the instant study in the two samples that they tested.

In a response to Bertram, Grupe presented sound scientific reasoning pointing out the deficiencies in the Bertram study, such as the difference between family-based samples and case-control samples, inadequacies of the characterization of controls in Bertram, etc. See Grupe, at page 183. Grupe concluded that Bertram's failure to "replicate our results does not necessarily indicate that the original association was a false-positive result", Grupe, at page 184.

Applicants have alluded to this reasoning in the previous response to office action, but that reasoning was dismissed as "attorney argument". See FOA, at page 7. It is important to note that, contrary to the Examiner's assertion that Applicants' analysis of the discrepancies between Bertram and the instant invention are mere "attorney arguments that cannot replace evidence on the record"

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(FOA, page 7), these discrepancies are evidence on the record as they are published in peer-reviewed journals, and cited in the office actions.

Therefore, the rejections under 35 USC §112, first paragraph, for allegedly lack of enablement have been overcome in light of the remarks above. The Pre-Appeal Brief Panel is respectfully requested to withdraw the rejections.

In conclusion, Applicants submit that the present application is fully in condition for allowance. Early notice to that effect is earnestly requested.

The Panel is invited to contact the undersigned via telephone if a phone interview would expedite the prosecution of the instant patent application.

Respectfully submitted,

By:



Ben Wang, Reg. No.: 41,420

Date: April 10, 2008

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